

# **Case 2. Choosing Wisely : FFR vs. Anatomy-guided Left Main PCI -The Rationale of the FATE-MAIN Trial**

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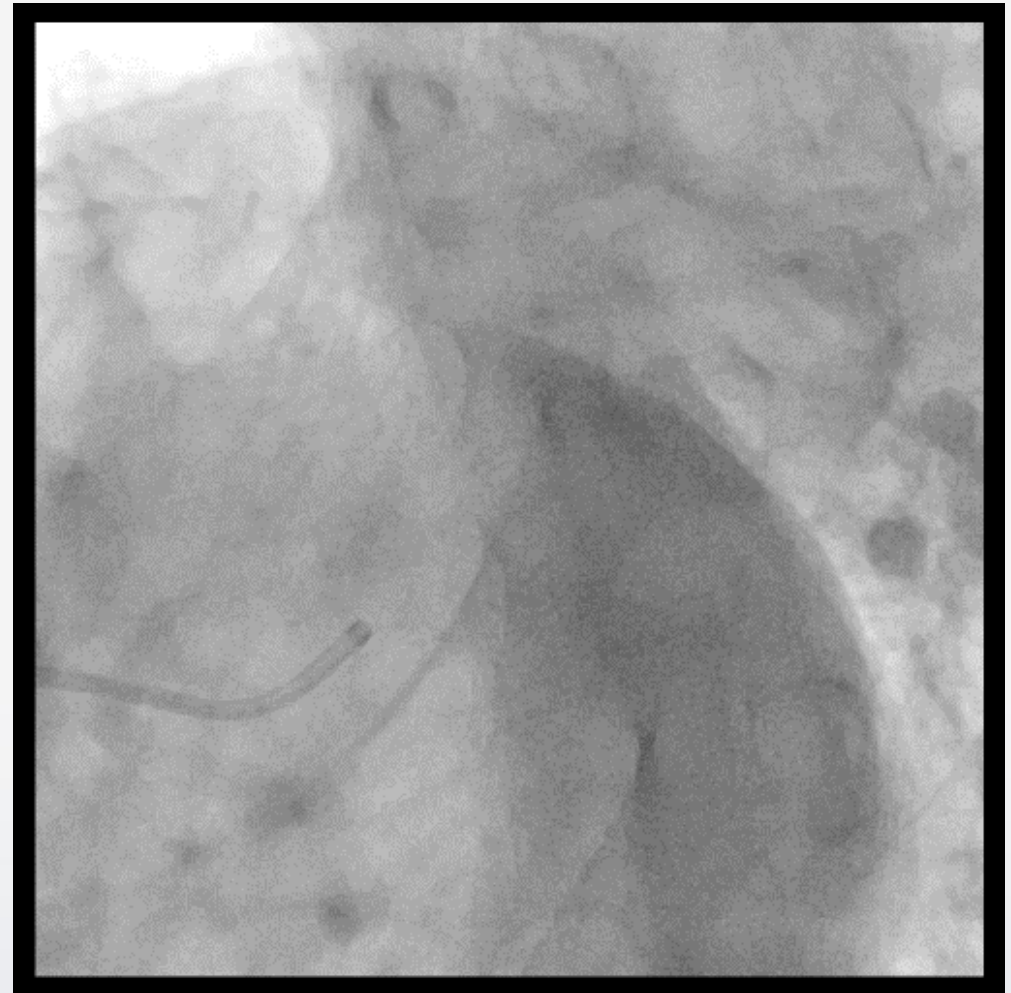
**TCTAP, 25 Apr 2024**

**COI Disclosure**

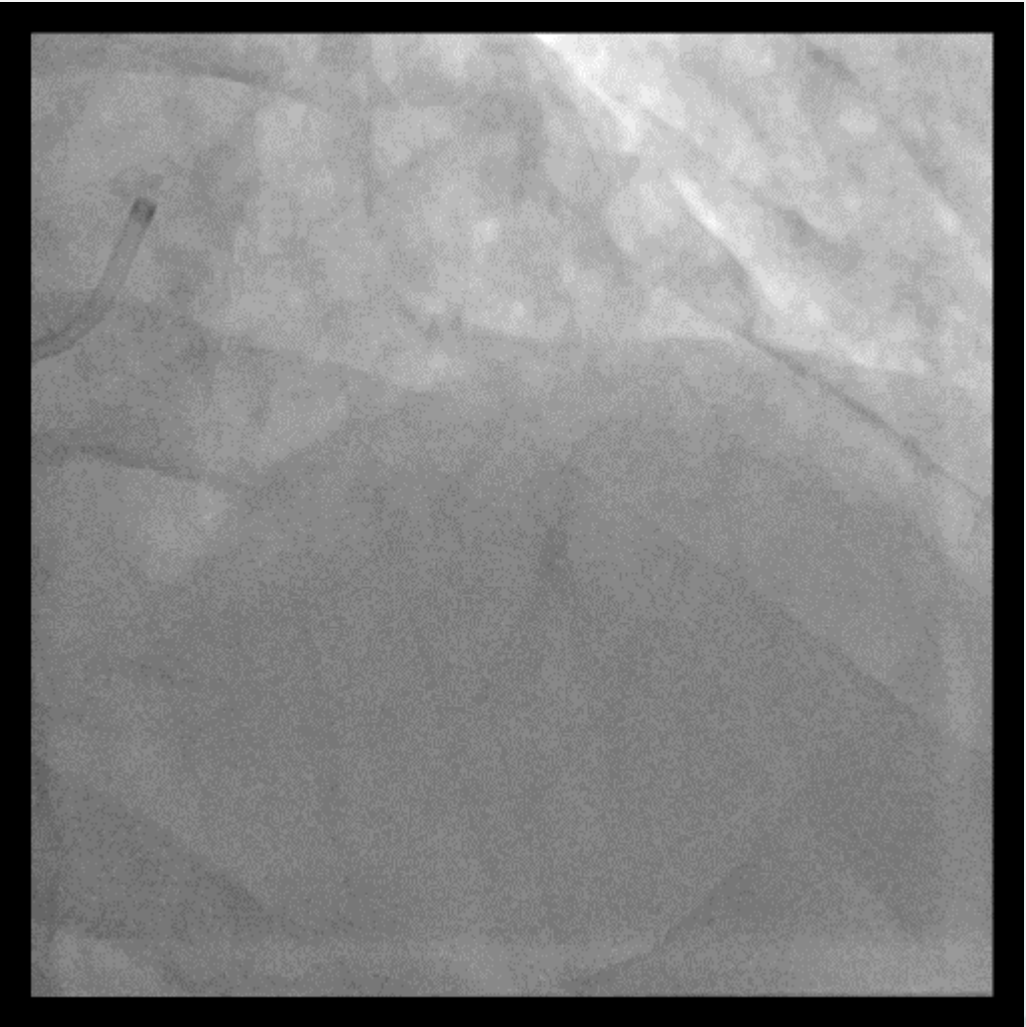
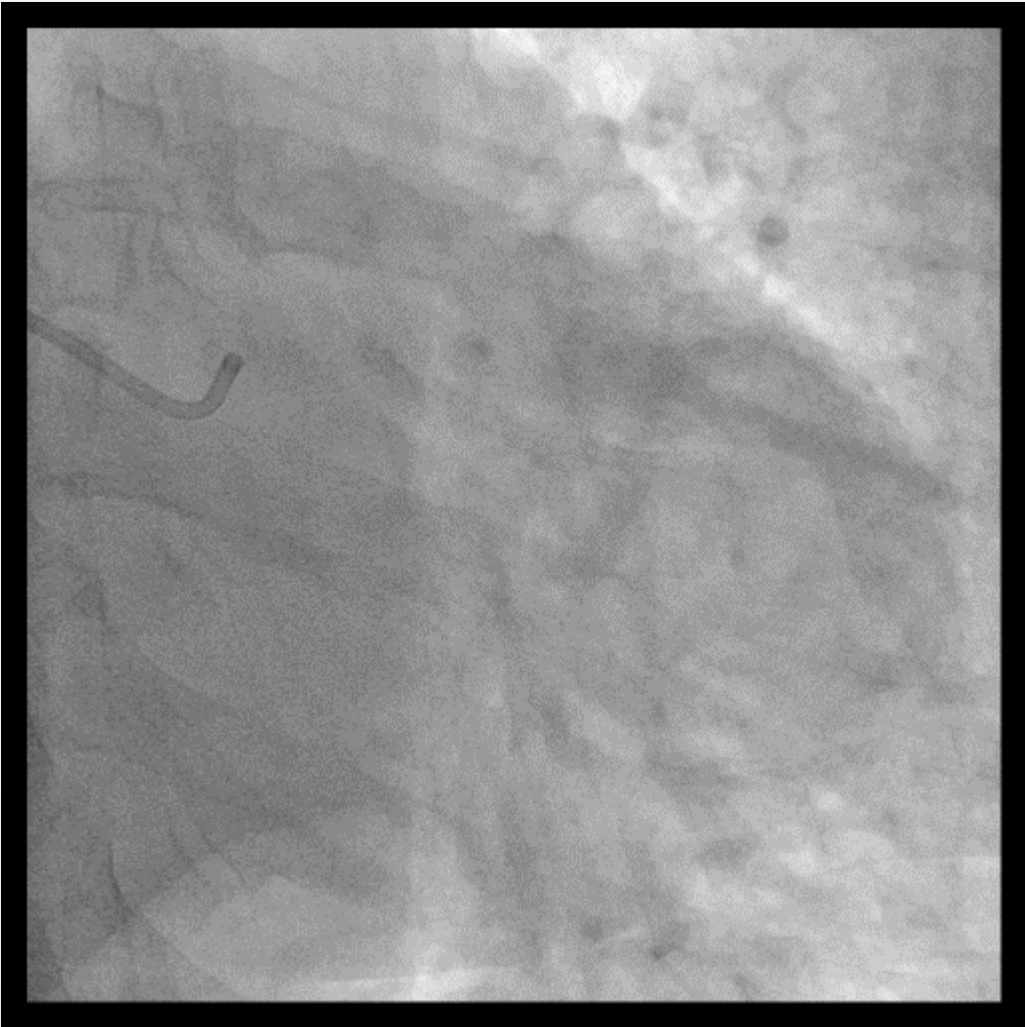
***Do-Yoon Kang***

- The author has no financial conflicts of interest to disclose concerning the presentation

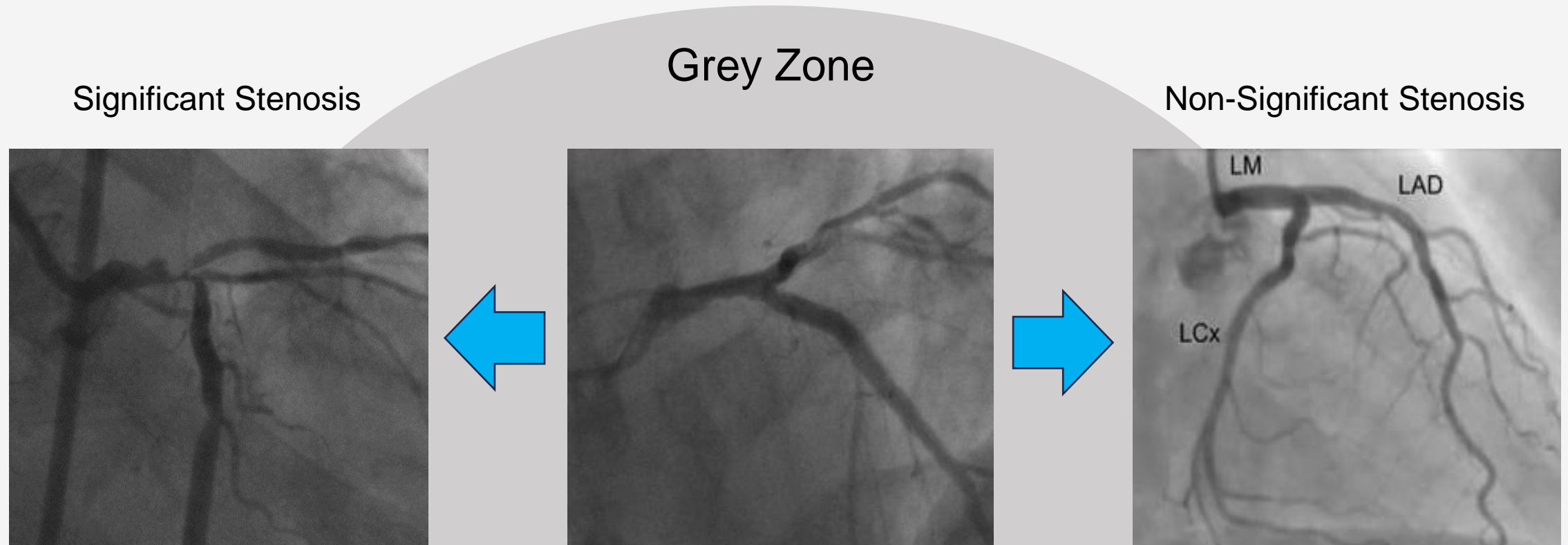
# A Live Case From This Morning : 73/F, Stable Angina



# A Live Case From This Morning : 73/F, Stable Angina



# What is the Significant Stenosis of LM ?



# Significant Left Main Disease (**DS>50%**)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Randomized Trial of Stents versus Bypass Surgery for Left Main Coronary Artery Disease

Seung-Jung Park, M.D., Young-Hak Kim, M.D., Duk-Woo Park, M.D., Sung-Cheol Yun, Ph.D., Jung-Min Ahn, M.D., Hae Geun Song, M.D., Jong-Young Lee, M.D., Won-Jang Kim, M.D., Soo-Jin Kang, M.D., Seung-Whan Lee, M.D., Cheol Whan Lee, M.D., Seong-Wook Park, M.D., Cheol-Hyun Chung, M.D., Jae-Won Lee, M.D., Do-Sun Lim, M.D., Seung-Woon Rha, M.D., Sang-Gon Lee, M.D., Hyeon-Cheol Gwon, M.D., Hyo-Soo Kim, M.D., In-Ho Chae, M.D., Yangsoo Jang, M.D., Myung-Ho Jeong, M.D., Seung-Jea Tahk, M.D., and Ki Bae Seung, M.D.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812      DECEMBER 8, 2016      VOL. 375 NO. 23

## Everolimus-Eluting Stents or Bypass Surgery for Left Main Coronary Artery Disease

G.W. Stone, J.F. Sabik, P.W. Serruys, C.A. Simonton, P. Généreux, J. Puskas, D.E. Kandzari, M.-C. Morice, N. Lembo, W.M. Brown III, D.P. Taggart, A. Banning, B. Merkely, F. Horkay, P.W. Boonstra, A.J. van Boven, I. Ungi, G. Bogáts, S. Mansour, N. Noiseux, M. Sabaté, J. Pomar, M. Hickey, A. Gershlick, P. Buszman, A. Bochenek, E. Schampaert, P. Pagé, O. Dressler, I. Kosmidou, R. Mehran, S.J. Pocock, and A.P. Kappetein, for the EXCEL Trial Investigators\*

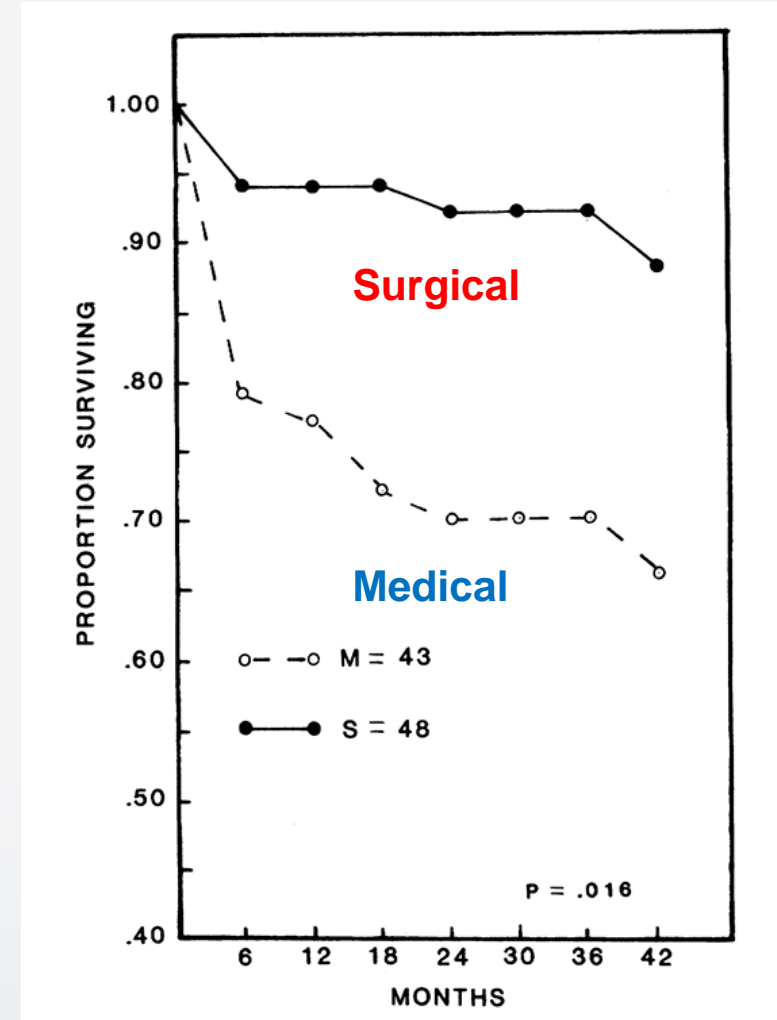
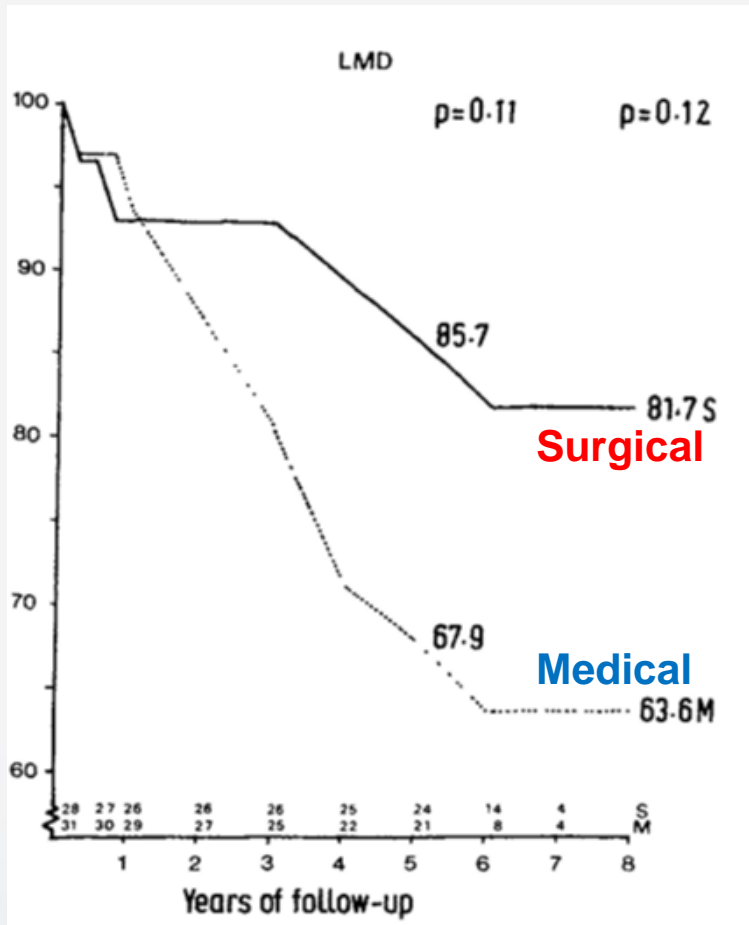
ABSTRACT

All patients had to have newly diagnosed unprotected stenosis of more than 50% of the diameter of the left main coronary artery, as estimated visually

Stenosis of the LMCA of 70% or more, as estimated visually, or stenosis of 50% to less than 70% if determined by means of noninvasive or invasive testing to be hemodynamically significant



# Significant Left Main Disease (**DS>50%**)



# Survival in Subgroups of LM

TABLE 4. Cumulative Survival Rates at 42 Months by Treatment Assigned (1972–1974 Left Main Lesion Cohort)

Group	n	Cumulative survival rate			Treatment† effect p	Homogeneity‡ p
		Medical	Surgical	Difference§		
All patients	91	0.65	0.88	0.23	0.016	
Stenosis 50–75%	47	0.82	0.92	0.10	0.089	0.47
> 75%	44	0.48	0.83	0.35	0.036	
LV function						
Normal	23	0.71	0.78	0.07	0.10	0.27
Abnormal	67	0.62	0.89	0.27	0.012	
Tercile*						
Low	33	0.93	0.83	-0.10	>0.50	0.035
Middle	24	0.58	0.92	0.34	0.073	
High	33	0.44	0.88	0.44	0.004	

\*Missing data on one patient for each factor.

†Test of overall difference in survival between treatment groups within a subgroup category.

‡Test of equality of treatment effects across subgroup categories.

§Surgical minus medical.

## Non-invasive Risk Factors

- History of MI
- History of Hypertension
- Resting ST depression
- NYHA III, IV

## Clinical Risk Subgroup

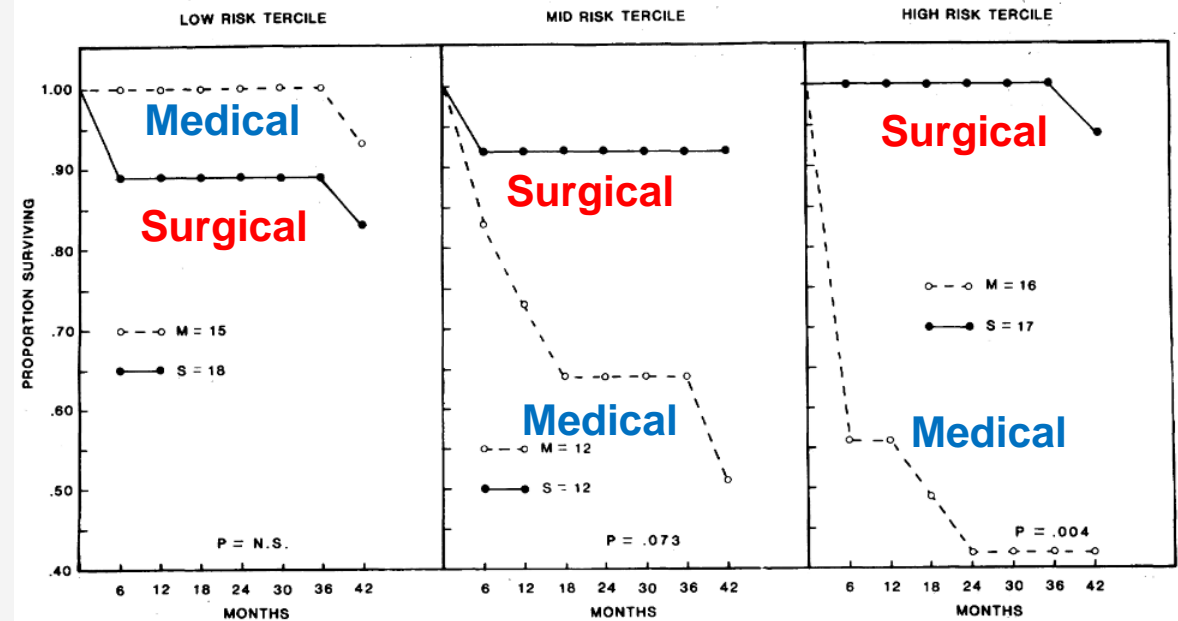


FIGURE 3. Cumulative survival rates in risk tertiles by treatment assigned. M = medical; S = surgical.



# Prognostic Spectrum of LM Stenosis

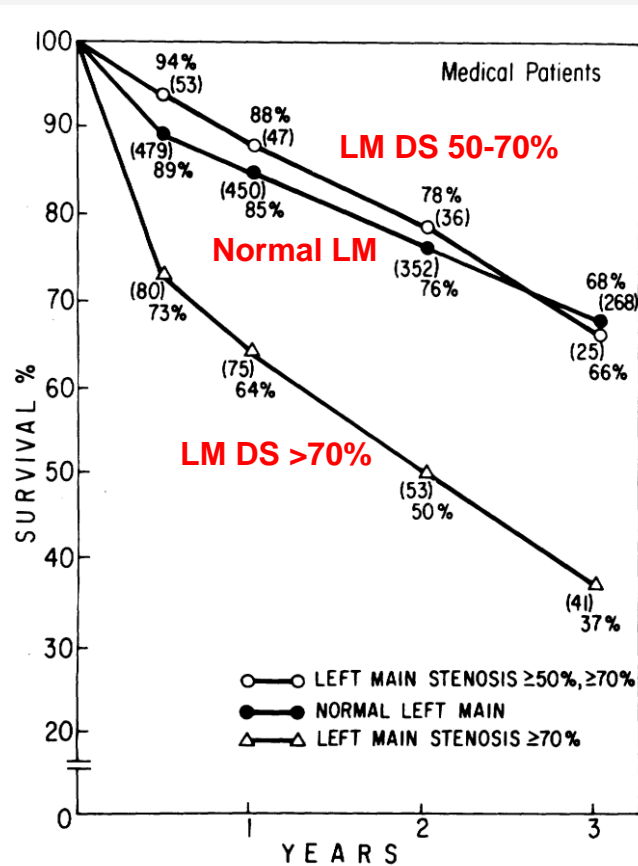


FIGURE 2. Cumulative survival rates of medically treated patients with three-vessel coronary artery disease who had a normal left main coronary artery, who had 50 to 70% left main stenosis, and who had 70% or greater left main stenosis.

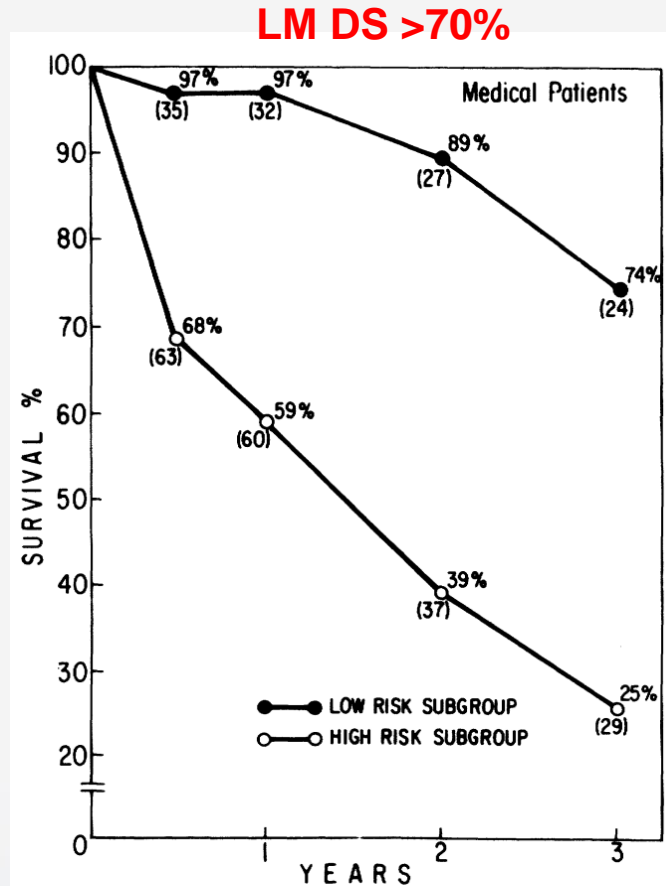
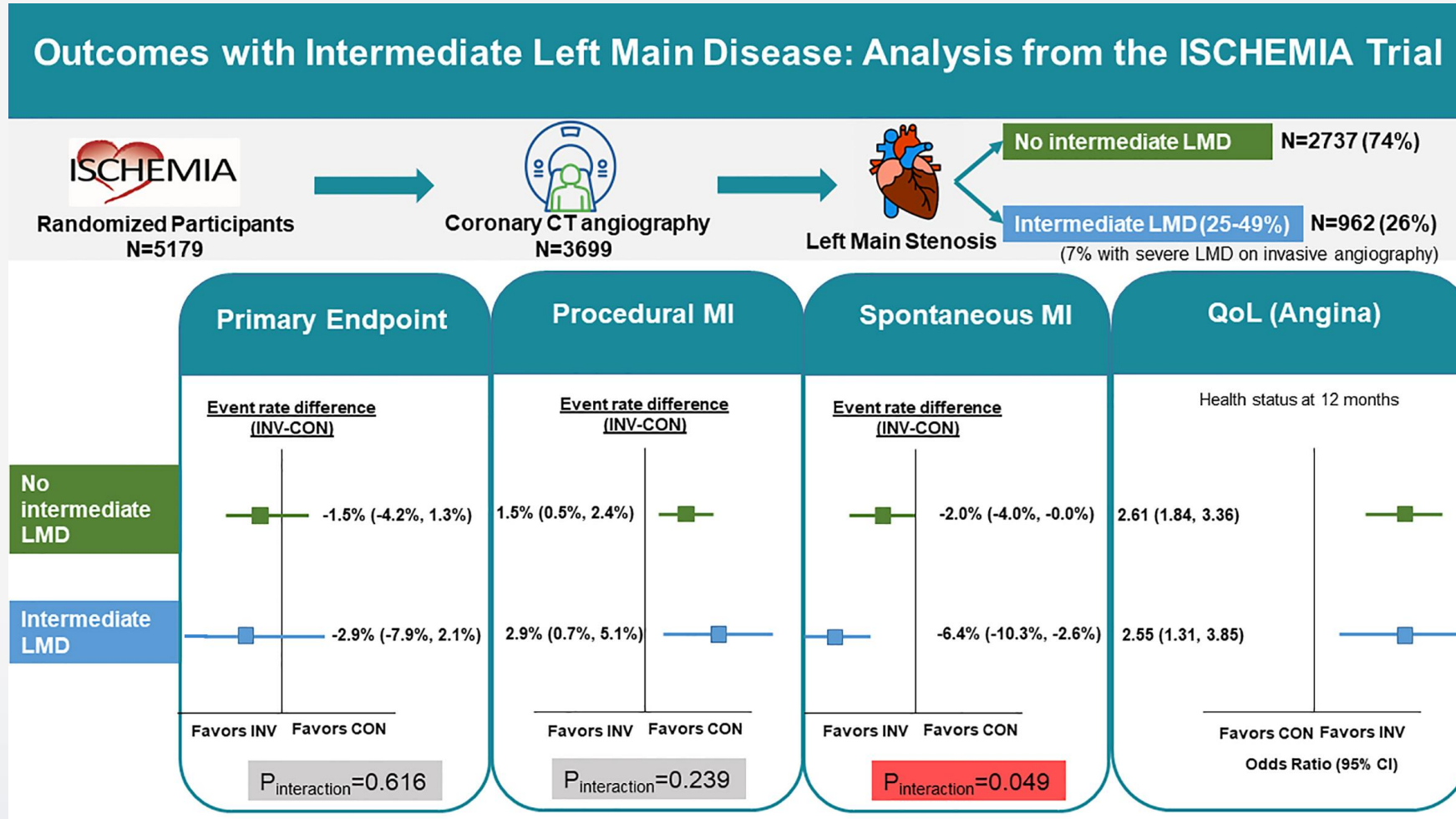


FIGURE 3. Cumulative survival rates of medically treated patients with 70% or greater left main stenosis divided into high and low risk subgroups on the basis of noninvasive characteristics.

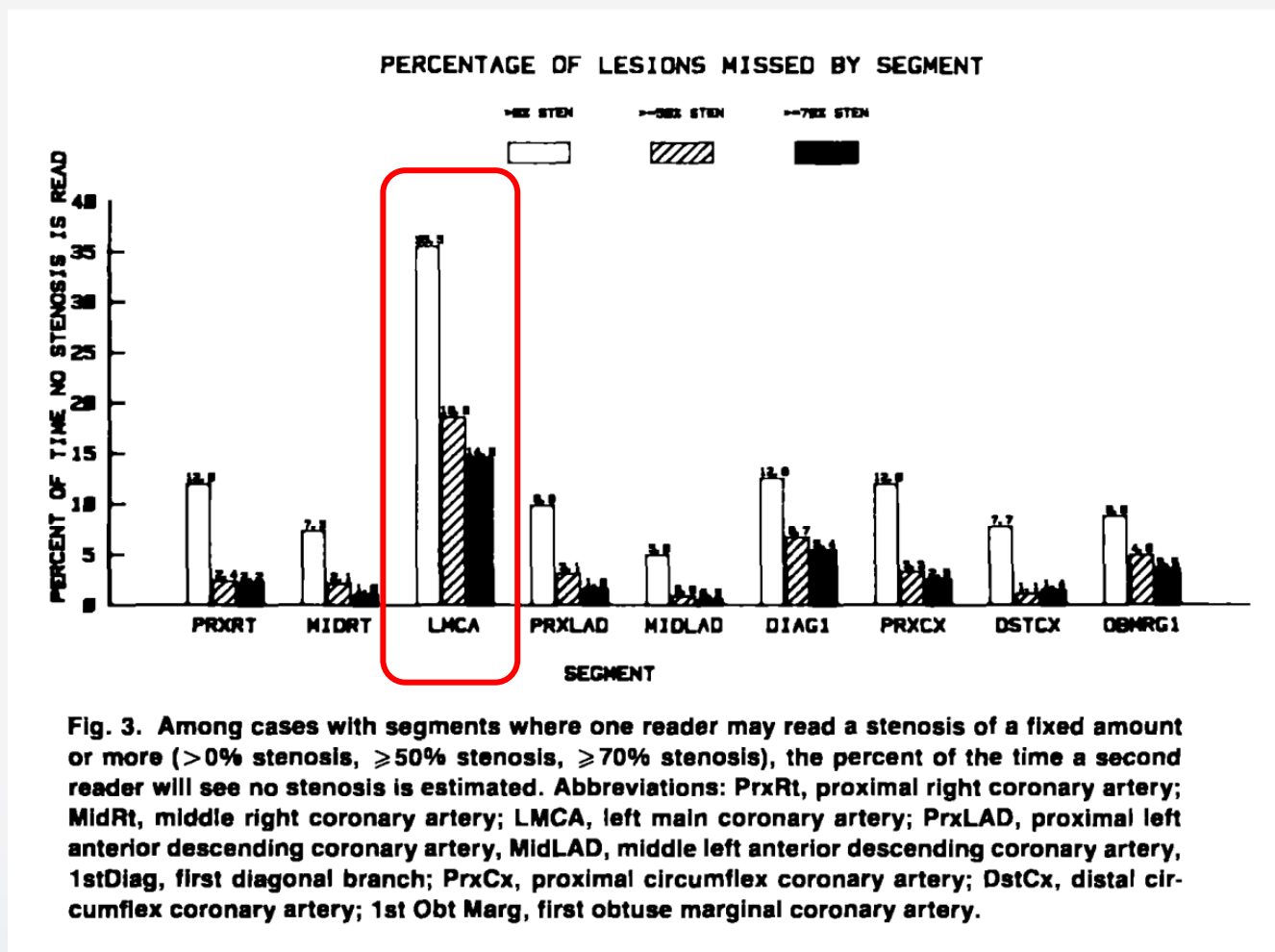
## Non-invasive Risk Factors

- History of congestive heart failure
- Chest pain at rest
- Cardiomegaly on chest X-ray
- ST-T wave change

# Intermediate LMD (DS, 25%–49%) on outcomes



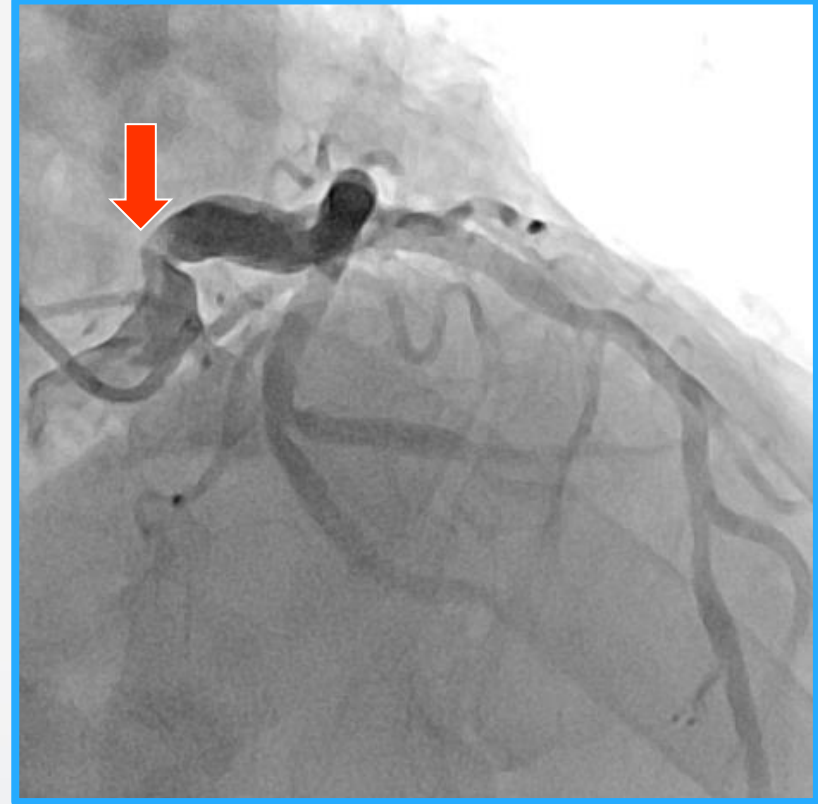
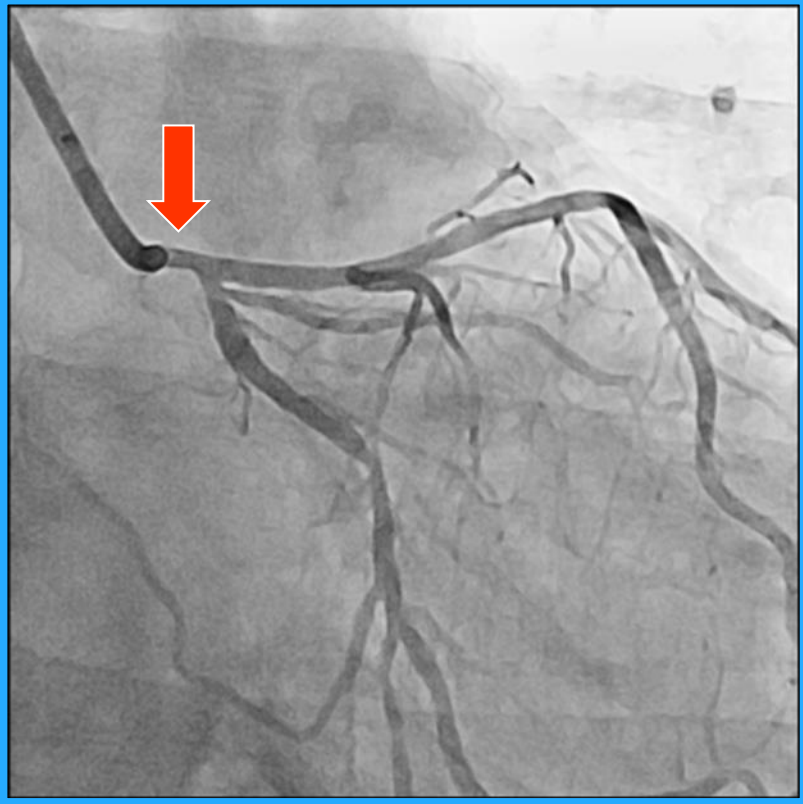
# CAG analysis for Left Main: **Poor** Reproducibility



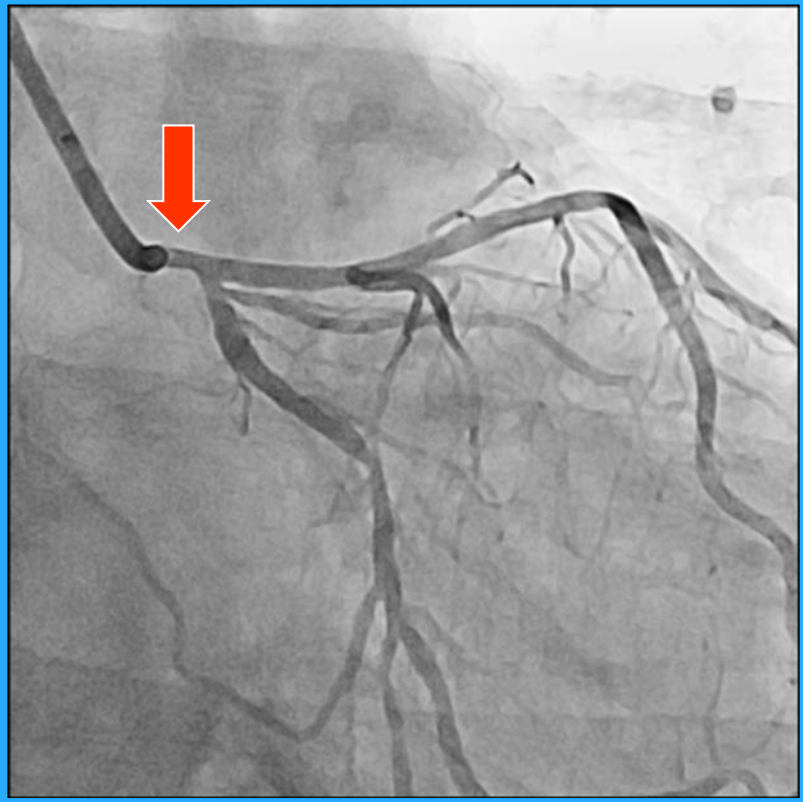
Reproducibility of coronary arteriographic reading in the coronary artery surgery study (CASS)

Fisher LD et al. Cathet Cardiovasc Diagn. 1982;8(6):565-75.

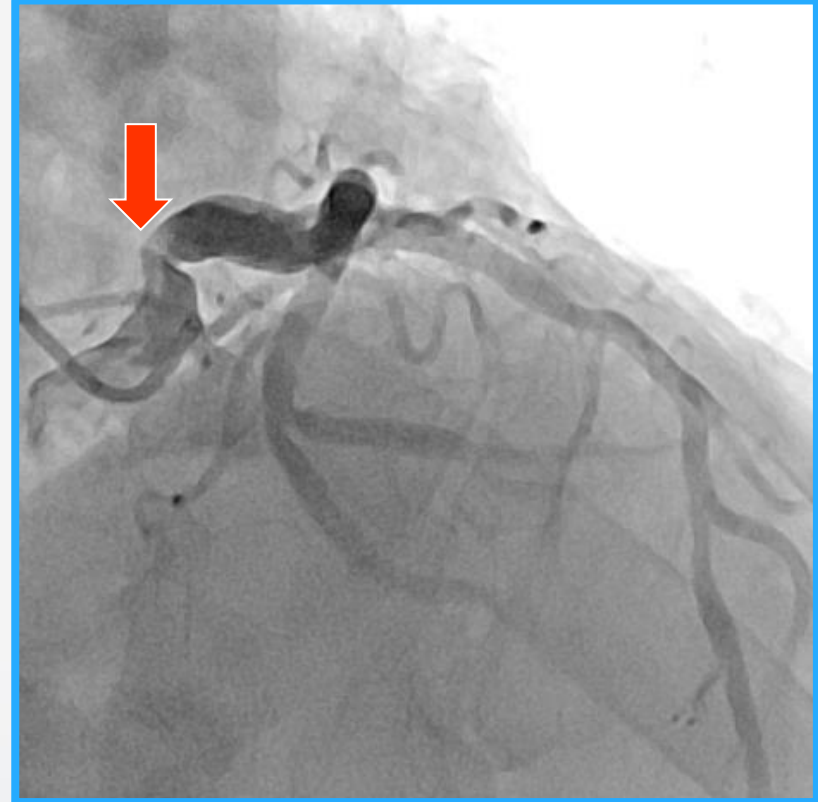
# Which is a Significant Stenosis ?



# Which is a Significant Stenosis ?



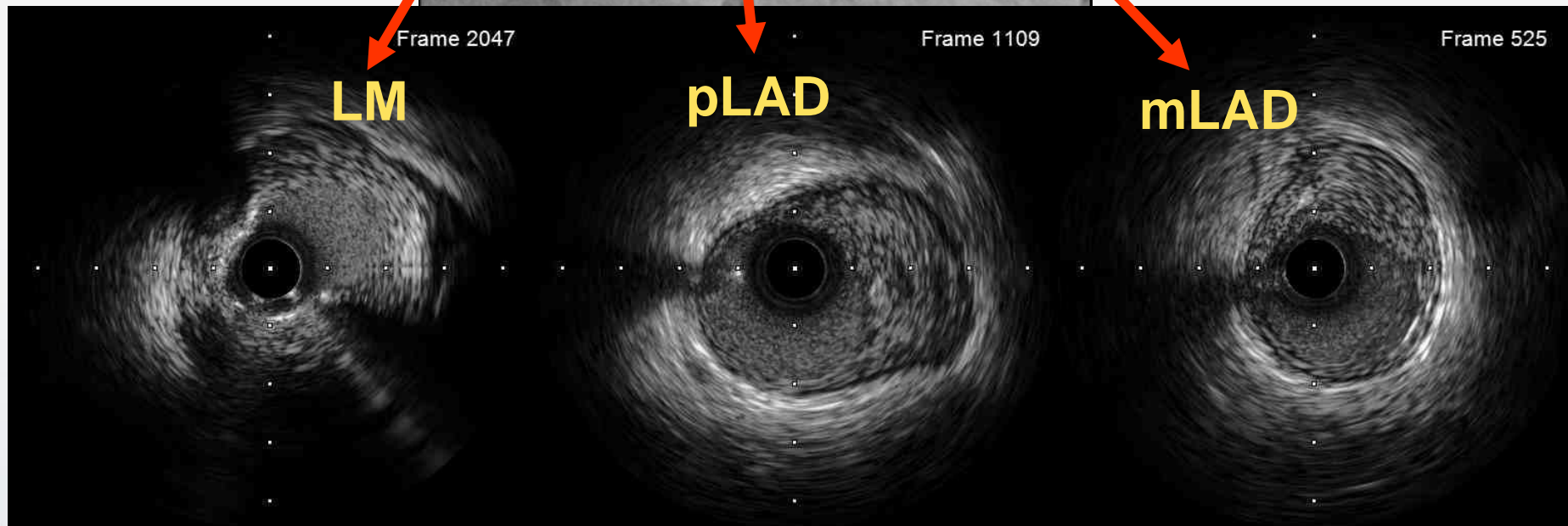
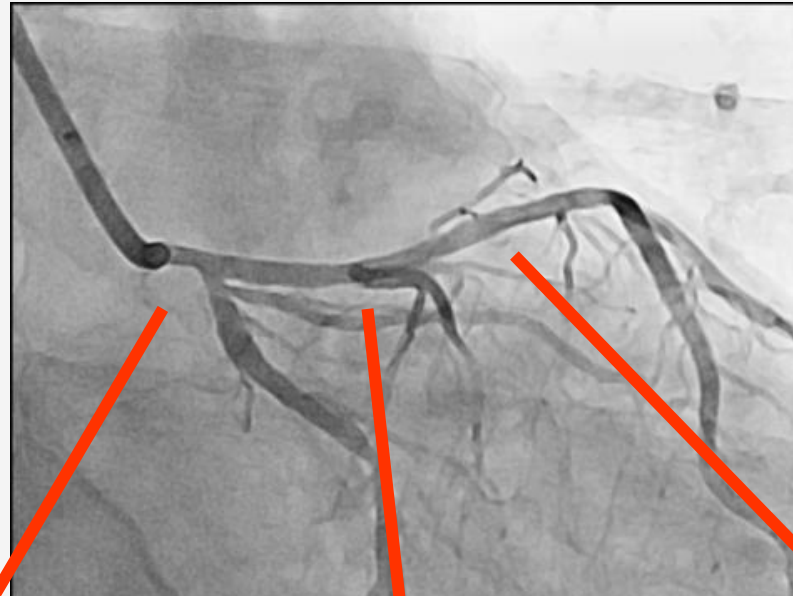
**FFR 0.71**



**FFR 0.89**

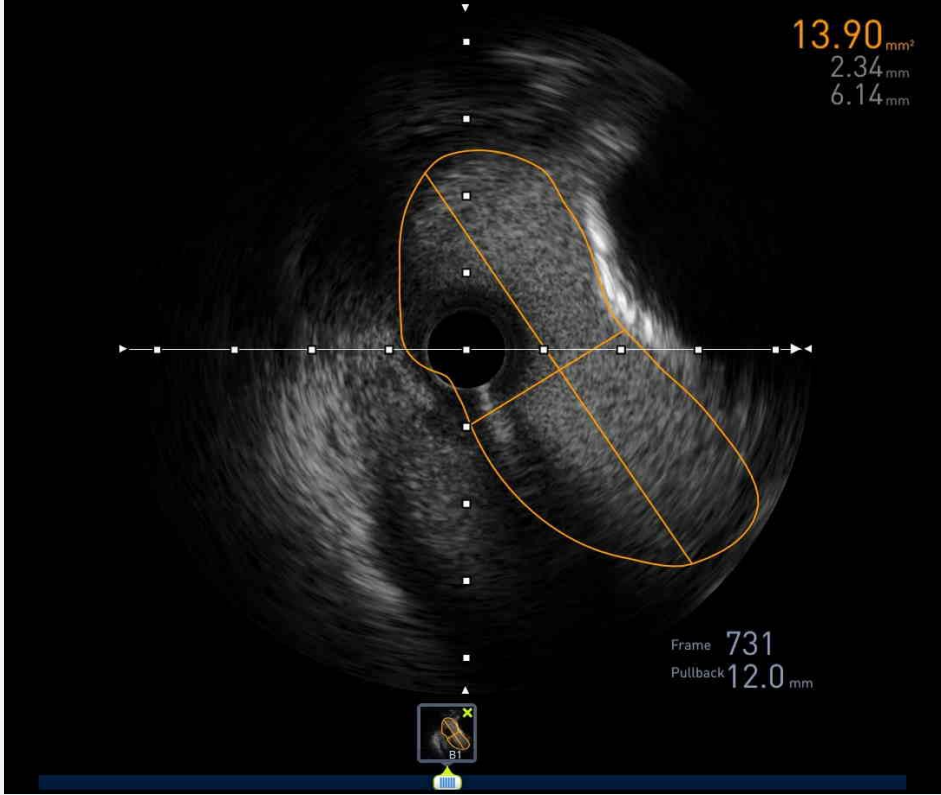
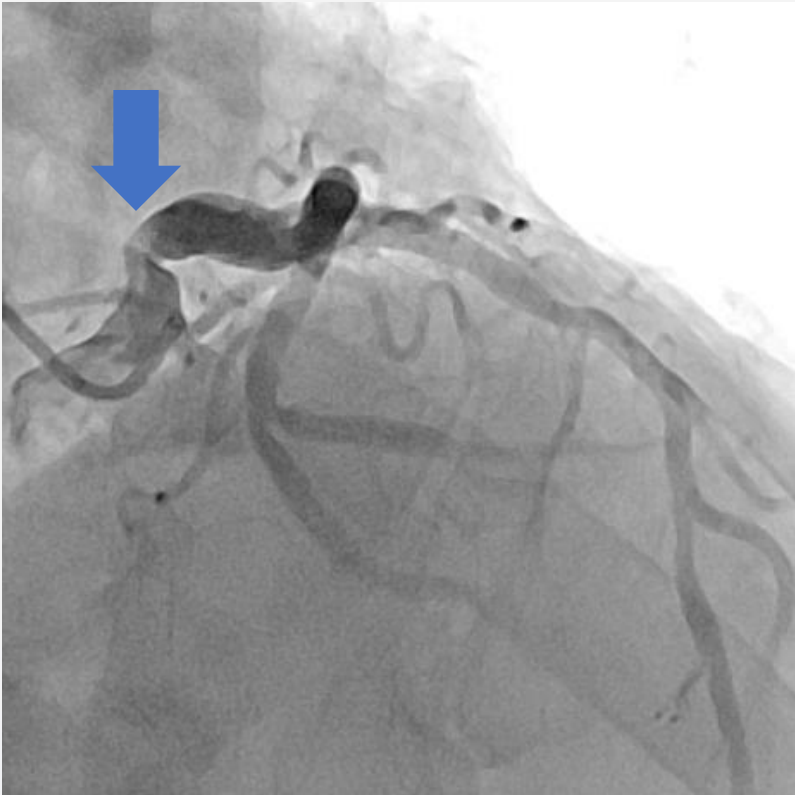


# Diffuse Atherosclerosis



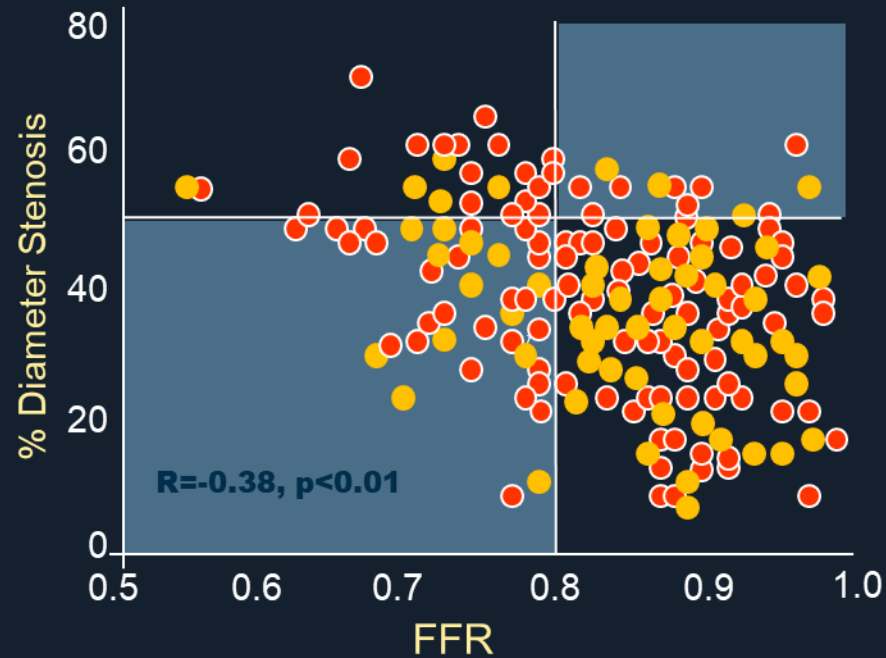


# MLA 8.8-13.9mm<sup>2</sup>



# Is the Coronary Angiography Accurate?

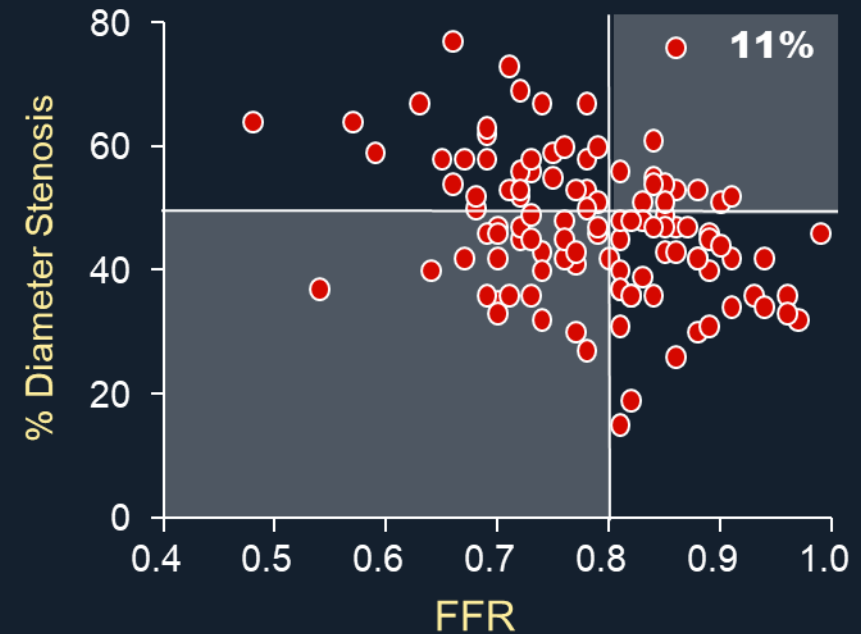
“Mismatch” is 29% in equivocal LMCA



Hamilos et al  
Circulation 2009;120:1505-1512

● Isolated LMCA disease

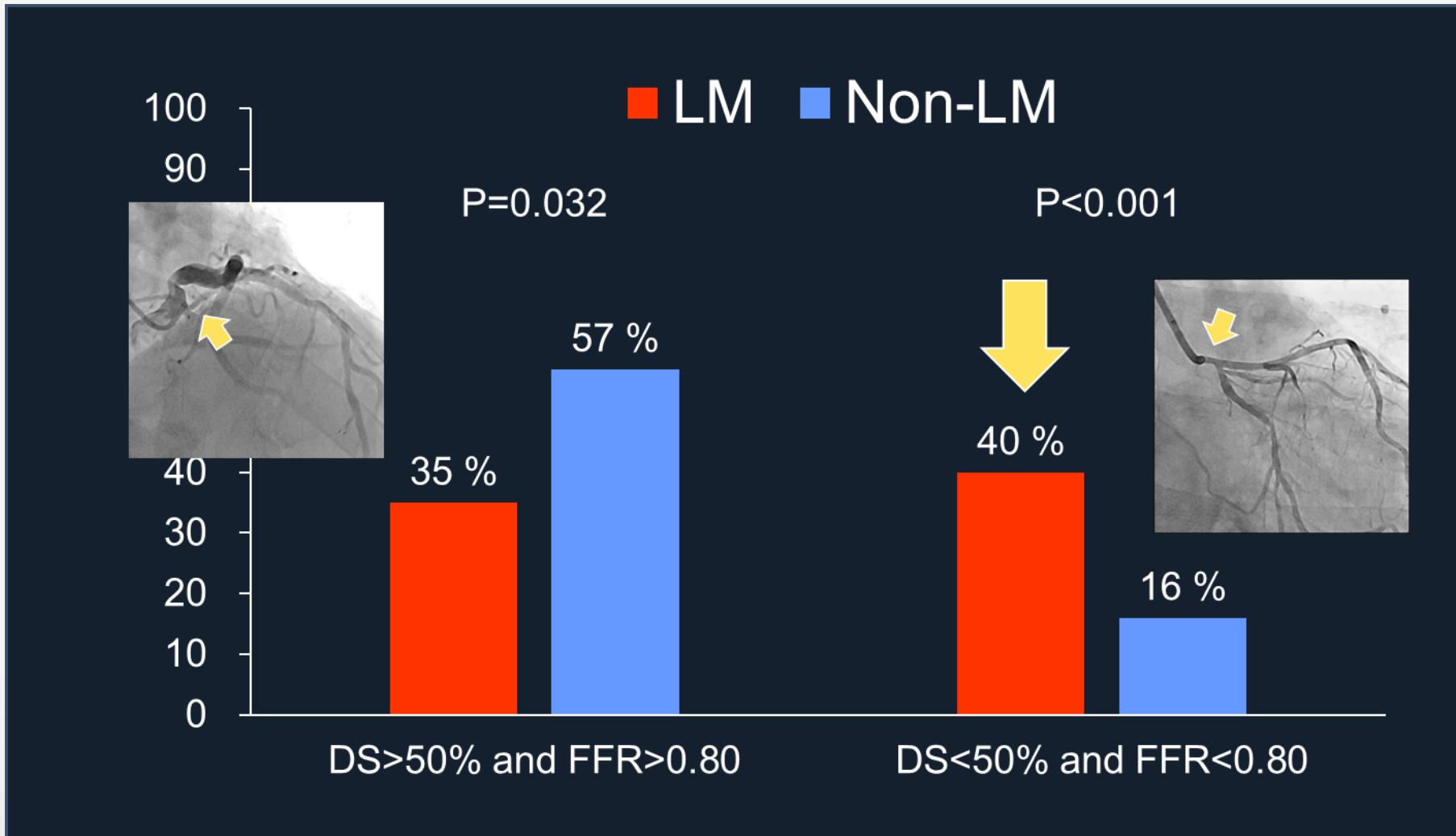
“Mismatch” is 37% in equivocal LMCA



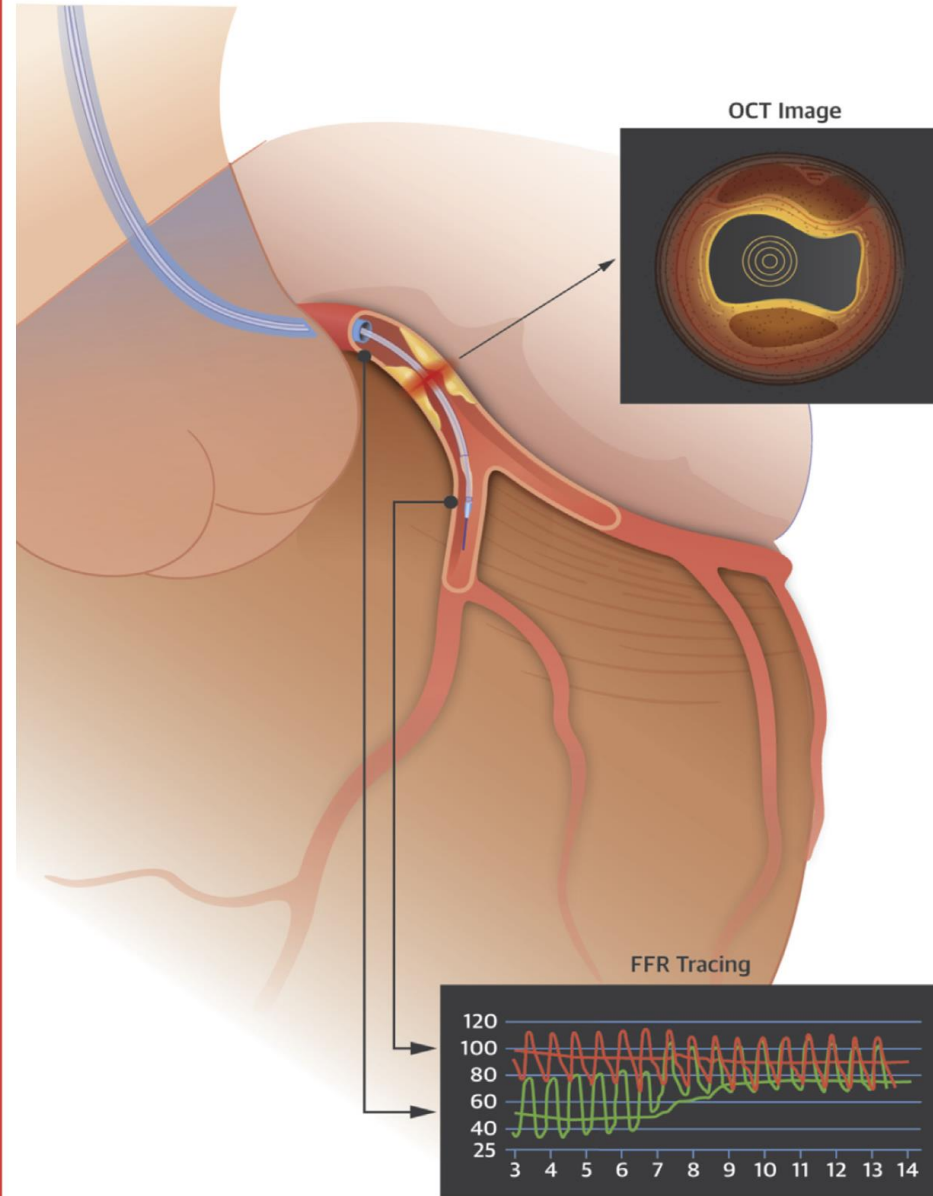
Park SJ, Ahn JM et al  
JACC Cardiovasc Interv. 2014 ;7(8):868-74

# Left Main Supplies Large Myocardium

In symptomatic patients, ambiguous LM stenosis should be evaluated by FFR



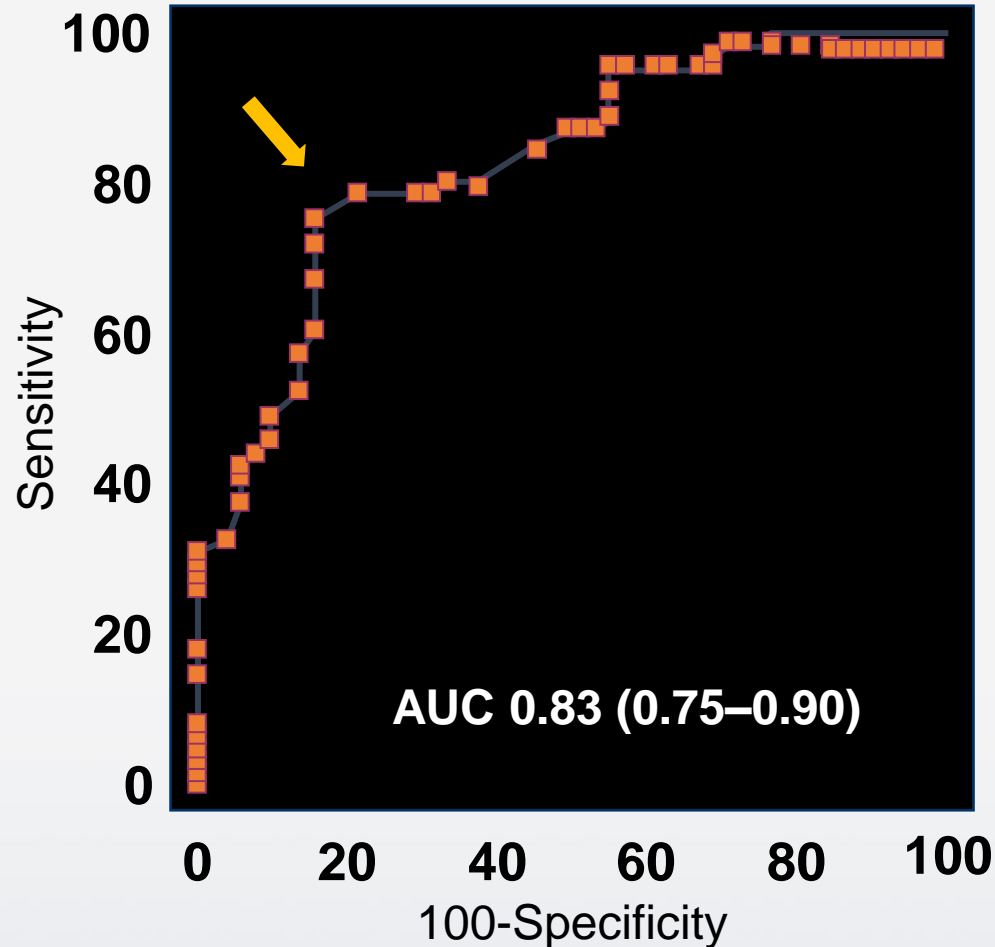
**CENTRAL ILLUSTRATION** OCT/FFR Evaluation of Moderate LMCA Lesion



Bing, R. et al. J Am Coll Cardiol Interv. 2015; 8(12):1529-39.

# LM IVUS MLA

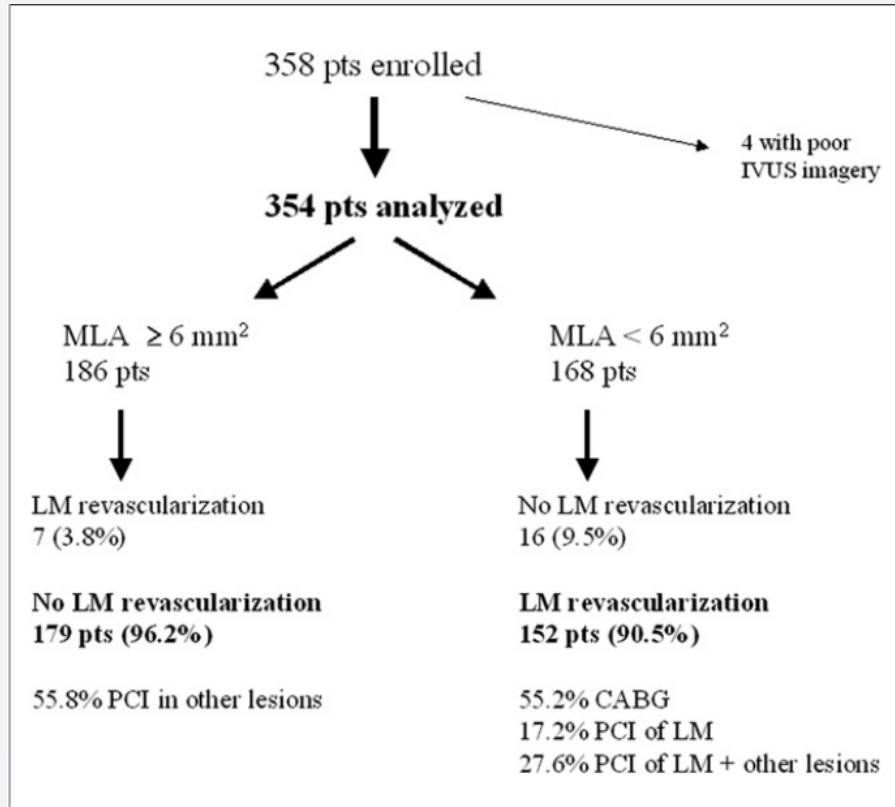
Matched with FFR <0.80 (N=112)



**Cut-off = 4.5 mm<sup>2</sup>**

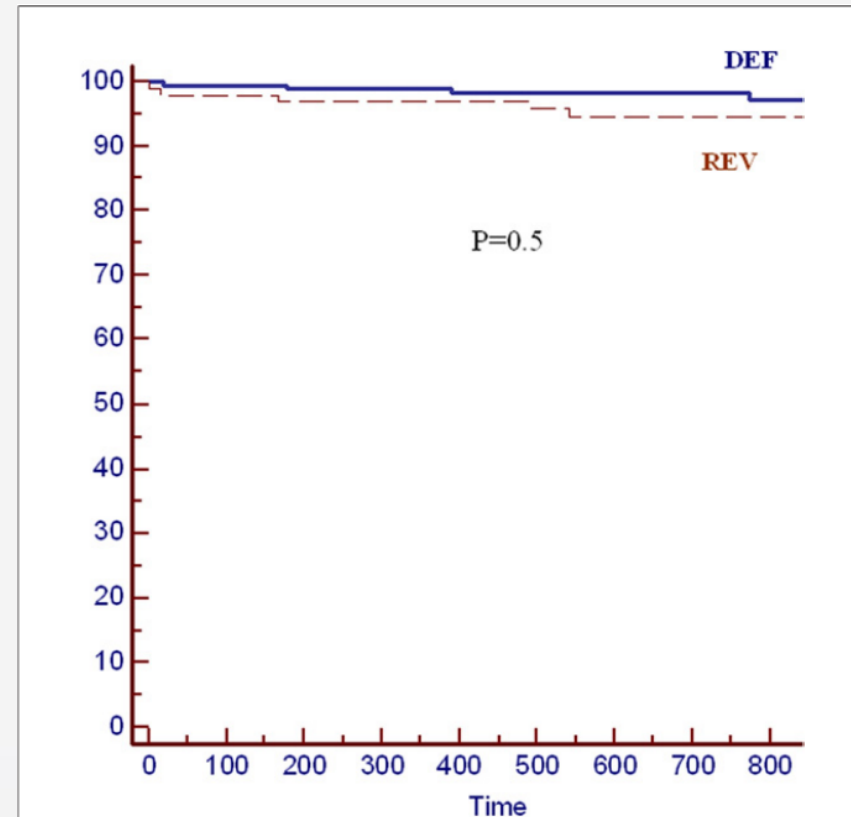
Sensitivity	79%
Specificity	80%
PPV	83%
NPV	76%
Accuracy	80%

# LITRO Study: Predefined MLA Criteria 6 mm<sup>2</sup>



**Figure 1** Flow Chart of the Study

CABG = coronary artery bypass graft; IVUS = intravascular ultrasound; LM = left main; MLA = minimum lumen area; PCI = percutaneous coronary intervention; pts = patients.



**Figure 4** Survival Free of Cardiac Death in Both Groups

Survival free of cardiac death in the deferred (DEF) and revascularized (REV) groups.



# 2018 ESC Guideline

## Recommendations on functional testing and intravascular imaging for lesion assessment

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
When evidence of ischaemia is not available, FFR or iwFR are recommended to assess the haemodynamic relevance of intermediate-grade stenosis. <sup>15,17,18,39</sup>	I	A
FFR-guided PCI should be considered in patients with multivessel disease undergoing PCI. <sup>29,31</sup>	IIa	B
IVUS should be considered to assess the severity of unprotected left main lesions. <sup>35-37</sup>	IIa	B

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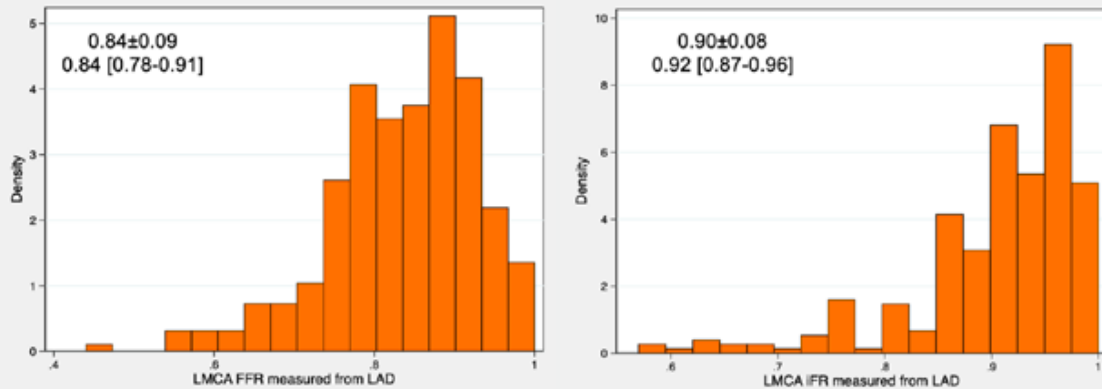
FFR = fractional flow reserve; iwFR = instantaneous wave-free ratio; IVUS = intravascular ultrasound; PCI = percutaneous coronary intervention.

<sup>a</sup>Class of recommendation.

<sup>b</sup>Level of evidence.

# iLITRO-EPIC06 : FFR / iFR in Intermediate (visual 25-65% DS) LMCA stenosis

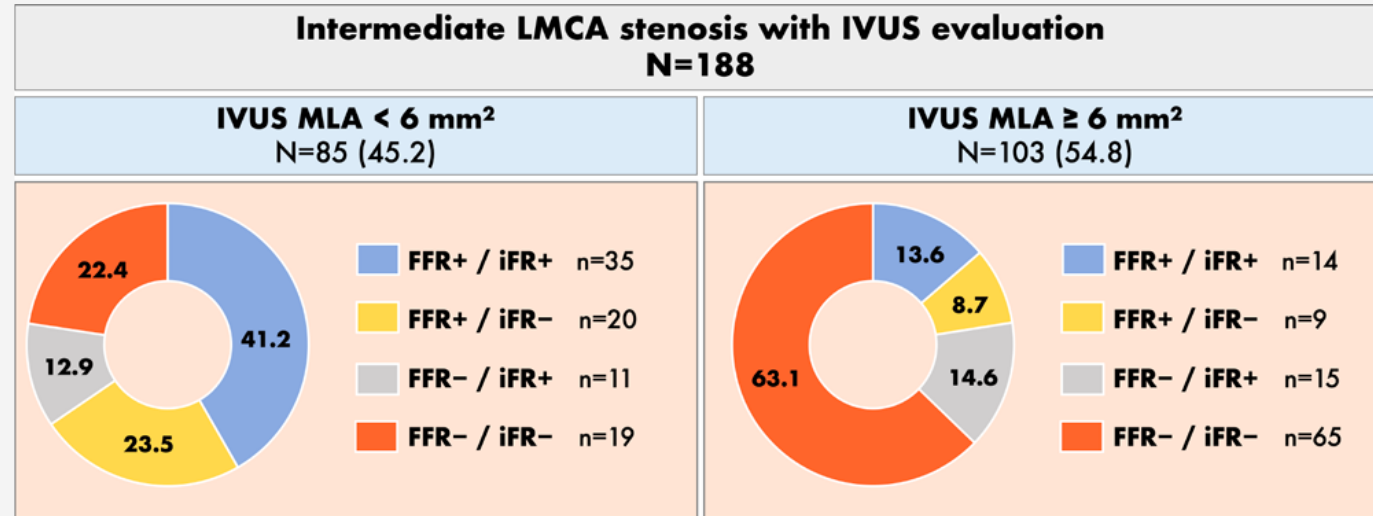
34% of patients had FFR  $\leq 0.80$



N=291  
Agreement 79.7%  
Kappa 0.54±0.06 (p<0.0001)

FFR	iFR		
	$\leq 0.89$	$> 0.89$	
$\leq 0.80$	23%	11%	34%
$> 0.80$	9%	57%	66%
	32%	68%	

35% of patients with IVUS MLA  $< 6 \text{ mm}^2$  had FFR  $> 0.80$   
22% of patients with IVUS MLA  $\geq 6 \text{ mm}^2$  had FFR  $\leq 0.80$



# Integrated use of FFR and IVUS in left main PCI

Park SJ et al. JAHA 2012  
Dec;1(6):e004556

## **Intermediate LMCA stenosis (DS\* 30-70%)**

### ***Ostial or Shaft Stenosis***

- **Whether to Treat or Not: FFR guidance**
  - FFR measurement is crucial
- **How to Treat: IVUS guidance**
  - Pre-intervention IVUS evaluation  
Evaluate minimal lumen diameter, reference vessel diameter, lesion length, plaque burden and distribution.
  - Pre-intervention IVUS optimization  
MSA<sup>‡</sup> >8.2mm<sup>2</sup> is important

### ***Bifurcation Stenosis***

- **Whether to Treat or Not: FFR guidance**
  - FFR measurement is important  
Consider a bifurcation stenosis as a single unit of disease (see Figure 2.)
  - IVUS can assist the functional evaluation of bifurcation stenosis  
MLA<sup>†</sup>>4.8mm<sup>2</sup> (sensitivity 89%, specificity 83%) and plaque burden>72% (sensitivity 73%, specificity 79%) to predict FFR≤0.80 (see Figure 3.)
- **How to Treat: IVUS guidance**
  - Pre-intervention IVUS evaluation  
Evaluate anatomic features favoring single stent cross over stenting (see Table 4.)
  - Post-intervention IVUS optimization  
Evaluate MSA in every segment of LMCA (see Figure 5.)

\* Visual estimated diameter stenosis; † Minimal lumen area; ‡Minimal stent area

# Clinical Outcomes After Deferral of LM Disease

## (6 studies, 296 patients)

<b>Outcomes</b>	<b>Incidence (%/year)</b>
<b>All Death</b>	<b>2.6 (1.3-5.2)</b>
<b>Cardiac Death</b>	<b>2.6 (1.3-5.2)</b>
<b>Myocardial Infarction</b>	<b>2.0 (0.7-5.1)</b>
<b>TVR</b>	<b>5.5 (3.3-8.8)</b>
<b>MACE</b>	<b>8.2 (5.5-12.1)</b>

Hamilos M, Circulation. 2009;120:1505-1512

Bech GJ, Heart. 2001;86:547-552

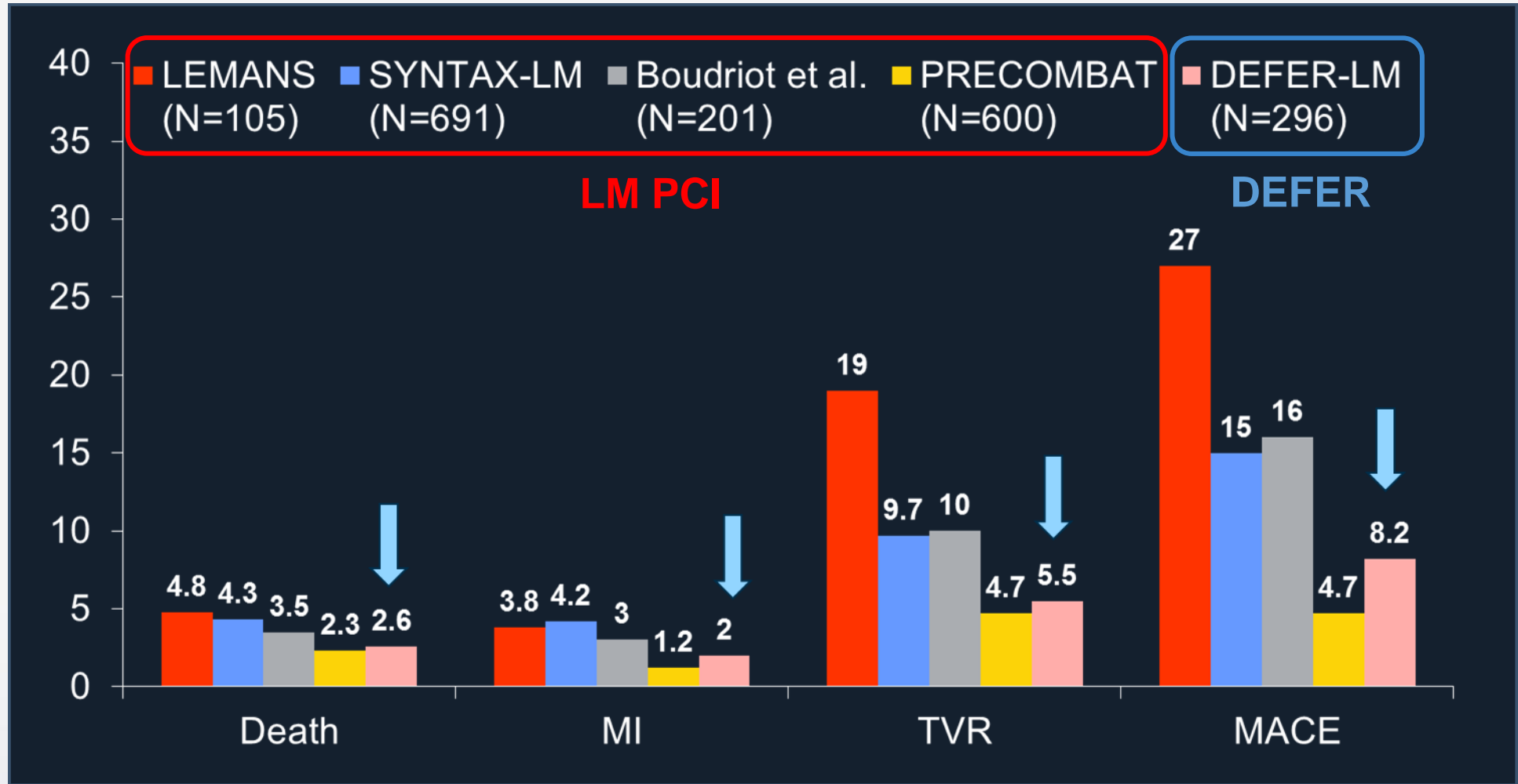
Courtis J, Am J Cardiol. 2009;103:943-949

Lindstaedt M, Am Heart J. 2006;152:151-159

Jasti V, Circulation. 2004;110:2831-2836

Sueman, Heart Vessels. 2005;20:271-7

# Safety of Deferred LM Disease



**F**ractional Flow Reserve versus **A**ngiography for **T**reatment-Decision and  
**E**valuation of Significant Left **MAIN** Coronary Artery Disease

# FATE-MAIN Trial

**934 Patients with Significant (Angiographic Diameter Stenosis  $\geq 50\%$ )  
Left Main Coronary Artery Disease Who Were Eligible for PCI**

1:1 randomization stratified by (1) participating sites and (2) the presence of concomitant non-left main PCI

**FFR-Guided Left Main PCI  
(N = 467)**

**Angiography-Guided Left Main PCI  
(N = 467)**

The primary end point was the composite of death from any cause, myocardial infarction, hospitalization for unstable angina, heart failure, or resuscitated cardiac arrest, or repeat revascularization at 2 years.



# Inclusion criteria

Inclusion Criteria: subject must have met all of the following criteria to be eligible for treatment in the study:

1. The subject must be  $\geq 20$  years of age with angina and/or evidence of myocardial ischemia
2. Significant de novo LMCA disease (defined as  $\geq 50\%$  diameter stenosis by visual estimation) with or without concomitant non-left main major epicardial CAD, amenable to PCI with DES implantation.
4. The patient or guardian agrees to the study protocol and the schedule of clinical follow-up, and provides informed, written consent, as approved by the appropriate Institutional Review Board/Ethical Committee of the respective clinical site.

# Exclusion criteria

1. Extremely calcified or tortuous vessels precluding FFR measurement
2. The presence of complex coronary disease anatomy or lesion characteristics or other cardiac condition(s) which leads the participating interventional cardiologist to believe that PCI is not suitable (i.e. the subject should be managed with CABG or medical therapy alone)
3. Recent STEMI (<7 days prior to randomization)
4. Cardiogenic shock and/or need for mechanical/pharmacologic hemodynamic support
5. Severe left ventricular dysfunction (ejection fraction <30%)
6. Requirement for other cardiac surgical procedure (e.g., valve replacement or aorta surgery)
7. Contraindication or inability to take aspirin or P2Y12 inhibitors (clopidogrel, ticagrelor, or prasugrel)
8. Prior PCI of the left main trunk
9. Prior CABG

# Study endpoints

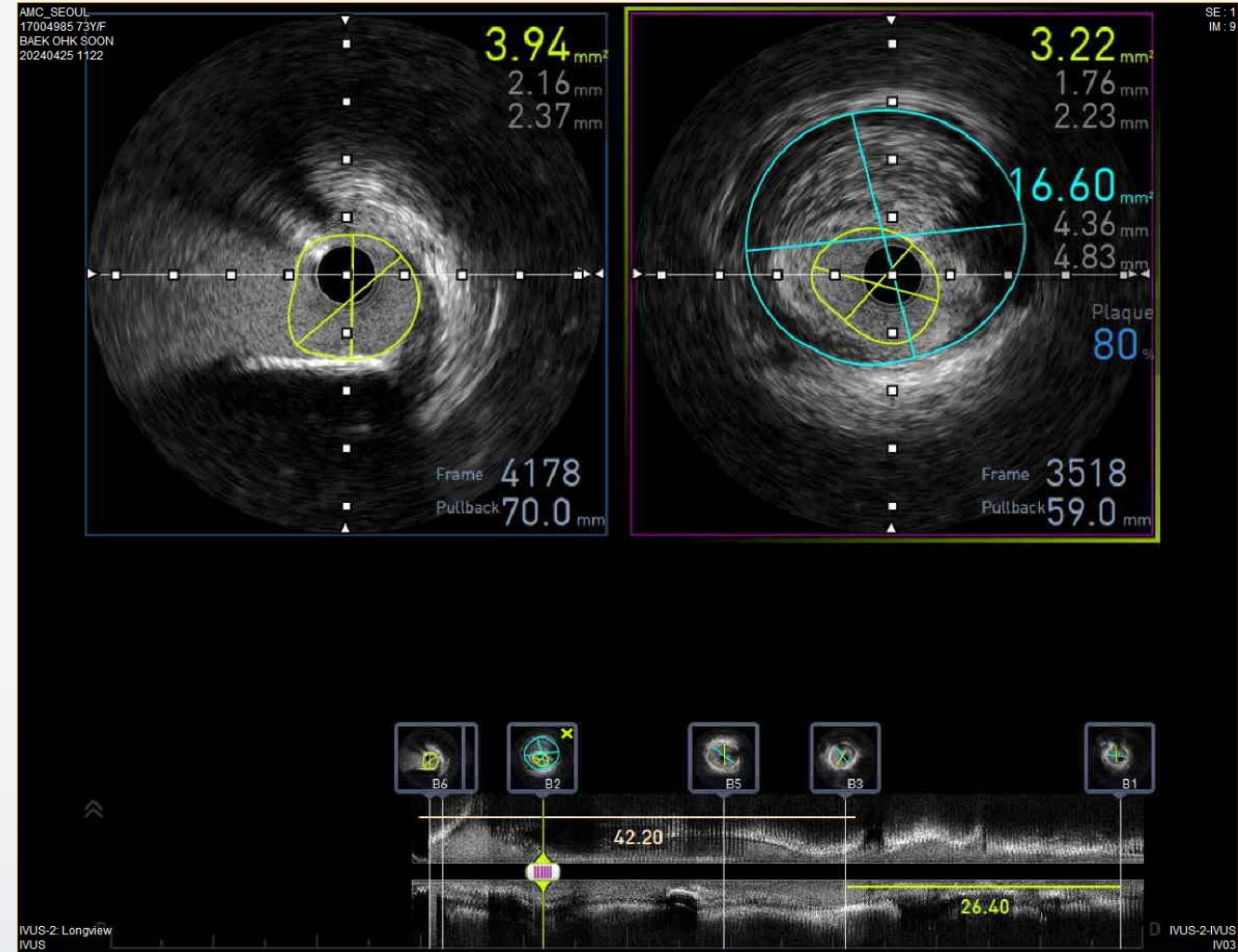
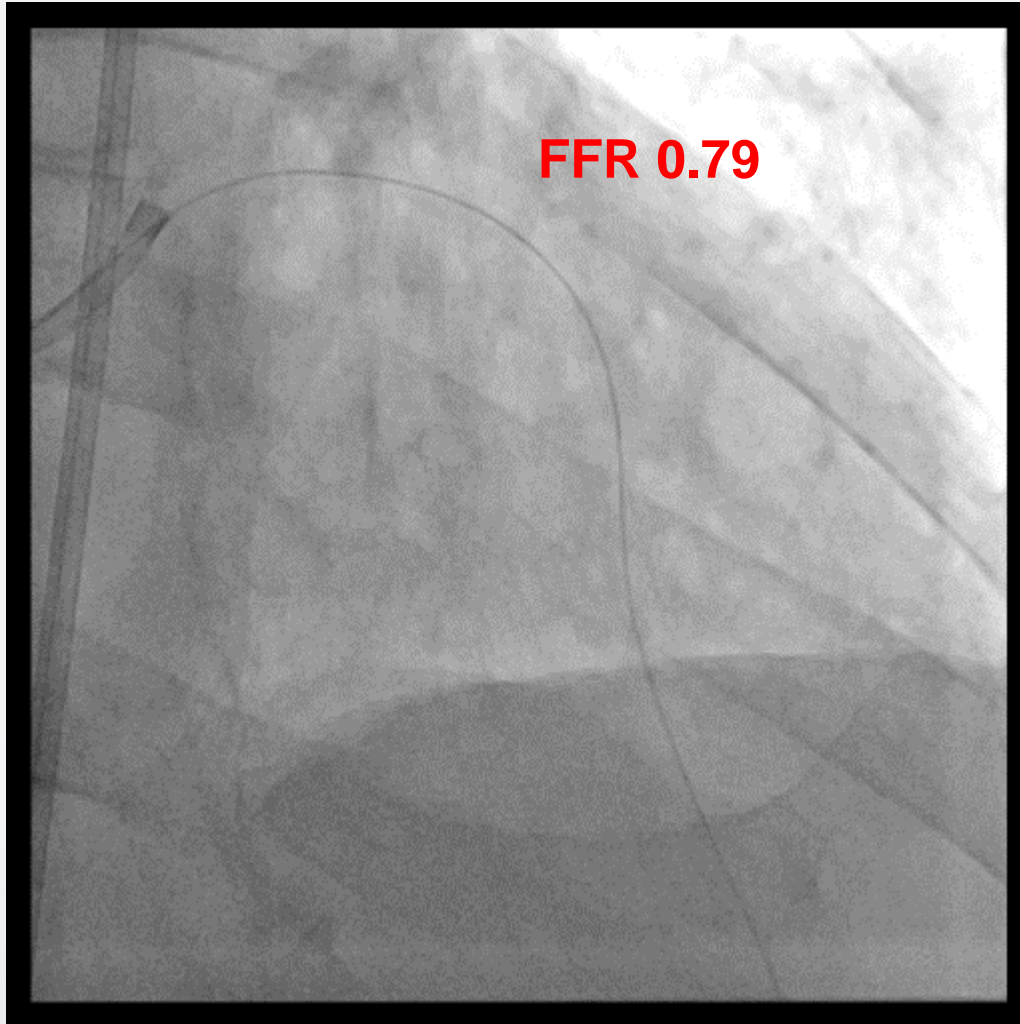
## Primary

The primary outcome was the composite of **death from any causes, MI, or hospitalization for unstable angina, heart failure, resuscitated cardiac arrest, or repeat revascularization** at 24 months after randomization.

## Secondary

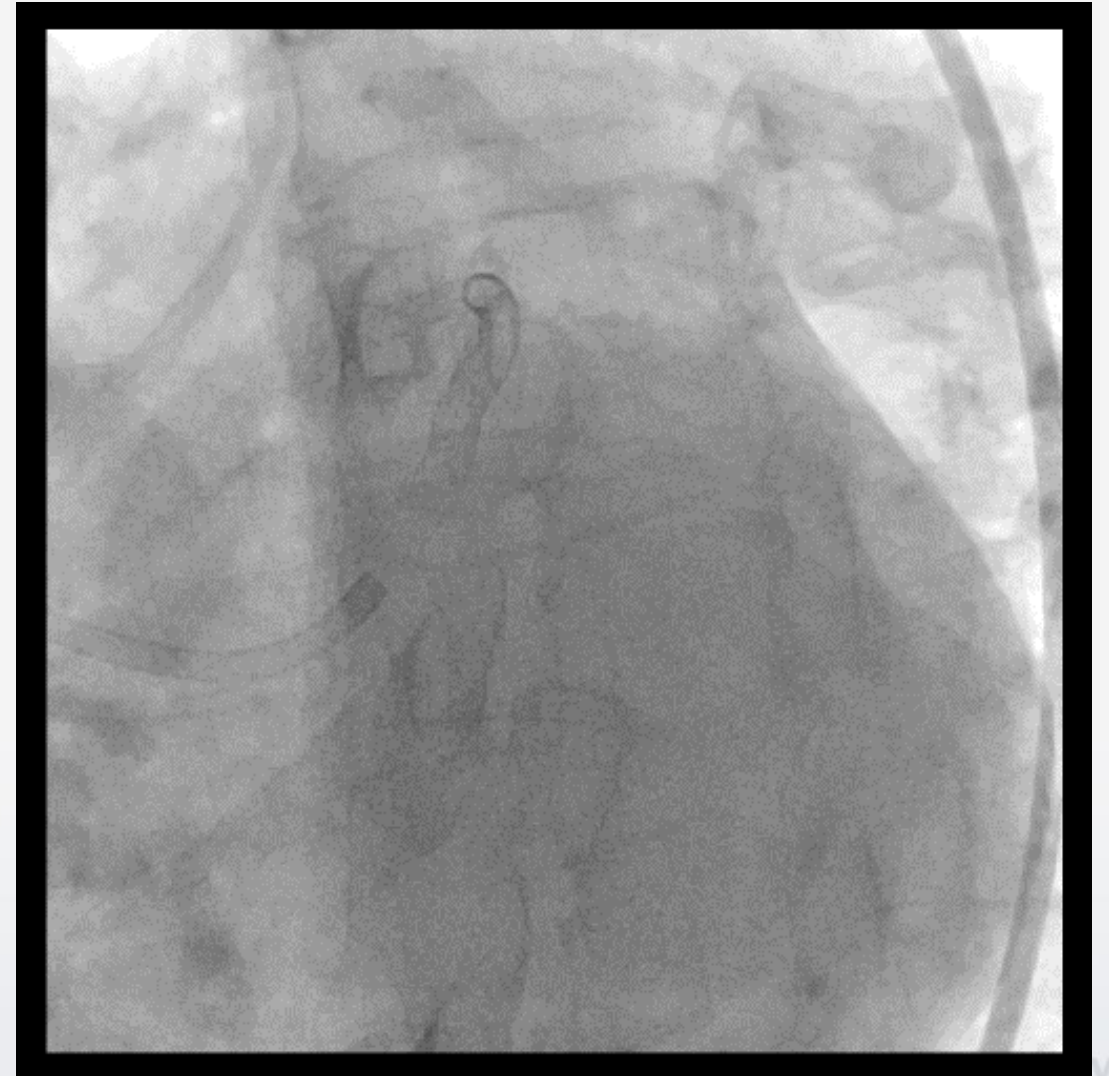
Each individual component of primary composite outcome; Composite of death or MI; Stent thrombosis (ARC definition); Bleeding complications (Bleeding Academic Research Consortium [BARC] criteria); Procedure time; Amount of contrast agent used; Length of hospital stay; Rehospitalization (any, cardiac, or noncardiac causes); Functional class (assessed by the CCS Classification); Angina-related quality of life index (by SAQ); Health-related quality of life index (by the EQ-5D); Number of anti-anginal medications used at each time point

# A Live Case From This Morning : After mLAD PCI





# A Live Case From This Morning : Final Results



# Key Messages

- In the contemporary clinical practice, the goal of PCI is to achieve complete functional revascularization of ischemic territories. Thus, theoretical and practical concept of physiology-guided PCI will also work even in left main PCI setting.
- For all “borderline or intermediate” LMCA, it is strongly recommended to confirm physiologic lesion significance before treatment using FFR evaluation and non-ischemia-producing lesions should not be treated.
- **In the FATE-MAIN trial**, we assume that the improved outcomes with FFR-guided PCI are likely a result of more judicious PCI whereby ischemia-producing LMCA lesions are revascularized and non-ischemia producing LMCA lesions are treated with OMT alone.